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**Harnessing the versatility of PLGA nanoparticles for targeted Cre-mediated recombination.**

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**Funding Grants:** Preclinical evaluation of human embryonic stem cell-derived cardiovascular progenitors in a large animal model

**Public Summary:**

Ligand-dependent Cre recombinases are pivotal tools for the generation of inducible somatic mutants. This method enables spatial and temporal control of gene activity through tamoxifen administration, providing new avenues for studying gene function and establishing animal models of human diseases. While this paved the way for developmental studies previously deemed impractical, the generation of tissue-specific transgenic mouse lines can be time-consuming and costly. Herein, we design a 'smart', biocompatible, and biodegradable nanoparticle system encapsulated with tamoxifen that is actively targeted to specific cell types in vivo through surface conjugation of antibodies. We demonstrate that these nanoparticles bind to cells of interest and activate Cre recombinase, resulting in tissue-specific Cre activation. This system provides a versatile, yet powerful approach to induce recombination in a ubiquitous Cre system for various biomedical applications and sets the stage for a time- and cost-effective strategy of generating new transgenic mouse lines.

**Scientific Abstract:**

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